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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/608,424
Filing Date: June 30, 2003
Appellant(s): FALO ET AL.

Stephen A. Bent
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12/26/07 appealing from the Office action mailed 1/26/06.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

The Examiner was affirmed in the appeal of U.S. Application No. 09/208,549.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The Appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The Appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner:

The rejection of Claims 1, 2, and 4-12 over Claims 1, 2, and 4-12 of U.S. Application No. 11/089,025 for obviousness-type double patenting has been withdrawn due to Appellant's election of a patentably distinct invention in the '025 application.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Frank, I. and Pope, M. The Enigma of Dendritic Cell-Immunodeficiency Virus Interplay. *Curr. Molec. Med.* 2002;2:229-248.

Roberts, J.P. Are HIV Vaccines Fighting Fire With Gasoline? *The Scientist*. 2004;18(11).

Stites, D.P., et al. *Basic and Clinical Immunology, Sixth Edition*. 1987;297.

Lewin, B. *Genes, Third Edition*. 1987;736.

Janeway, C.A. and Travers, P. *Immunobiology*. 1994;2.20-21.

Dictionary.com: http://dictionary.reference.com/browse/-oma.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 2, and 4-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for, a formulation comprising a hybridoma, said hybridoma comprising a DC and a tumor cell,

does not reasonably provide enablement for, a formulation comprising a hybridoma, said hybridoma comprising a DC and a virally infected cell.

A review of the specification reveals that the formulations of the instant claims are defined as "prophylactic and therapeutic agents against tumor and viral infection" (page 1), "can induce $CD8^+$ CTL" (page 3), and "protect against viral infection" (page 4). Clearly then, the formulations of the instant claims are pharmaceutical compositions and require enablement as such. The specification provides no teachings sufficient to enable claims drawn to a DC hybridoma which induces effective anti-virally-infected cell immunity. Note that the specification discloses background references and examples that deal *exclusively* with anti-tumor DC responses and anti-tumor DC hybridomas. Anti-virally-infected cell immunity is disclosed only in concept, a concept that was not enabled in 1997.

In the case of HIV infection the situation is even more unpredictable given the fact that both DCs and T cells are infected by the virus. As taught by Frank et al. (2002):

> "A dendritic cell (DC) encountering an immunodeficiency virus should pose a threat to the virus, by efficiently processing and presenting viral antigenic determinants to activate specific anti-viral T and B cell

> immunity. While this may occur *in vivo*, it is apparent that DC-entrapped viruses can freely spread between cells, move to distal tissues, and proliferate rapidly particularly upon meeting $CD4^+$ T cells. In fact, the latter is further augmented when the T cells are activated. Thus, it seems that immunodeficiency viruses exploit the unique ability of DCs to survey the periphery and capture incoming pathogens, traffic around the body often targeting the lymphoid tissues, and efficiently communicate with naive and memory T cells. Combined with the fact that DCs are likely the first leukocytes interacting with virions crossing the mucosae, these features provide the basis on which the virus maximizes its chance to establish infection even in the face of immune activation."

Given this teaching, it would seem then that the formulations of the instant claims would be more likely to exacerbate viral infections than to treat or prevent them. The reference further teaches that other viruses, including herpes simplex virus, measles virus, sendai virus, vaccinia virus, and cytomegalovirus infect DCS and down-modulate their antigen presenting functions. Accordingly, the use of the DC hybridomas of the instant claims to induce effective anti-virally-infected cell immunity would be highly unpredictable. Said unpredictability would then require undue experimentation in using the formulations of the instant claims *in vivo* as disclosed in the specification.

See also Roberts (2004, IDS); in a publication entitled, *Are HIV Vaccines Fighting Fire with Gasoline?*, the author teaches that activating T cells in an attempt to fight HIV may actually exacerbate disease. The reference notes that HIV preferentially infects, and grows better in, activated T cells (a concept known as of the priority date of the instant application). Clearly then, given the very basic questions still to be answered as recently as 2004, the formulations of

the instant claims were at best highly unpredictable and requiring of undue experimentation as of the 1997 priority date.

Also note that the claims are drawn to at least one "hybridoma". As taught by Stites et al. (1987), a hybridoma comprises, "a transformed cell line grown *in vitro* that is a somatic hybrid of 2 parent cell lines". Note particularly the term "transformed". As taught be Lewin (1987) "transformed" is defined as "a state of unrestrained growth in culture, resembling or identical with the tumorigenic condition". As can be seen in Janeway et al. (1994) it is the immortal tumor cell that contributes the ability to grow indefinitely to a hybridoma. Returning to the instant invention comprising a mortal DC and a mortal virally-infected cell, it is clear that neither the mortal DC nor the mortal virally-infected cell is capable of contributing transformation/immortality to the claimed formulation, thus, in addition to failing to teach how to use the claimed formulation for its intended use (as set forth above), the specification also fails to teach how to make the "hybridoma" of the instant claims. Given the failure of the specification to teach how to make and how to use the formulation of the instant claims, said formulation is considered to be highly unpredictable and requiring of undue experimentation.

A review of the specification shows that *no* examples of hybridomas comprising a DC and a virally-infected cell are disclosed, i.e., no such formulations are made and none are shown to have any biological or pharmacological activity.

Accordingly, as set forth above, it is the Examiner's position that the specification fails to enable one of skill in the art to make or use the DC/virally infected cell formulations of the instant claims.

Applicant is advised that simply stating that the hybridoma comprises "a physical combination of at least two different cell types" and that said hybridoma can be made by "any method known in the art", including using PEG, does not comprise an enabling disclosure. For the reasons set forth previously it is unclear that a such a fusion would result in a "hybridoma", or that whatever the fusion product would comprise, that it would be effective for its intended use.

Marañon et al. comes some seven years after the priority date of the instant application, thus, it cannot be used to establish the enablement of the instant application as of its priority date. Second, the reference employs live antigen-loaded dendritic cells and not the fusion products of the instant claims. Also note that the reference addresses a number of issues that were clearly not known as of the priority date of the instant application, in particular, the manner in which dendritic cells take up and present antigens (note the use of the terms "unexpectedly" and "surprisingly"), a property that it is unclear whether or not the fusion products of the instant claims would possess.

Regarding Applicant's assertion that the formulations and compositions and need not be enabled for treating all viral infections, a product must be enabled for its intended use. As

set forth at page 4 of the instant specification, the claimed formulations "protect against the viral infection caused by the virally infected cells used in the formulation, and/or provide therapeutic relief from patients having such viral infections". Also note that a formulation specifically comprising HIV is recited in claim 4. Further note that the compositions referred to by Applicant are actually "pharmaceutical compositions" (Claims 8-12). Clearly, the only intended use for the products of the instant claims is the treatment of viral infections, a use that is not enabled by the instant specification.

(10) Response to Argument

Appellant begins by broadly alleging that the Examiner has discounted enabling evidence. In addition, "the Examiner has failed to demonstrate that the entire claim scope is enabled". Finally, Appellant argues that the examiner has focused on a single HIV embodiment of the invention.

Enabling evidence has not been discounted; the specification simply discloses none. Regarding the scope of enablement, it most certainly is *not* the Examiner's burden to demonstrate that the invention is enabled. Said burden is Appellant's. Regarding the HIV embodiment, said embodiment is claimed and provides a meaningful example of why the claimed formulation is not enabled.

Appellant argues that the specification contains working examples demonstrating the formation of a hybridoma.

The specification contains *no* examples demonstrating the formation of a hybridoma comprising a DC and a virally infected cell. *All* of the examples comprise a DC and an immortalized tumor cell.

Appellant argues that the claims do not require that the hybridoma be an immortal cell, further arguing that, "applicant is entitled to be his or her own lexicographer".

"Hybridoma" has a clear definition in the art - a hybridoma is a "hybrid" of a normal cell and an "oma", "oma" being Greek for a tumor cell (see the teachings of Stites et al. (1987) and Lewin (1987) as set forth in the rejection teaching the immortality of tumor cells). Additionally, see the Dictionary.com collection of four different definitions of the term "-oma", all of which require that an "-oma" comprise a tumor cell. Turning to the "definition" of hybridoma disclosed at page 6 of the specification, it is readily apparent that the "definition" therein does not redefine the term. The redefinition of such a well-known term would require a clear statement that the Applicant was intending to use a definition that would be contrary to that known in the art, i.e., that the "hybridoma" of the claims does *not* comprise a tumor cell. Such a statement is not found in the specification; the specification merely discloses that a hybridoma can also be virally infected (virally infected tumor cells being known in the art). The specification does *not* disclose that a hybridoma consisting of an APC and a virally infected cell that is not actually an "oma", i.e., a tumor cell, is intended to be encompassed by the term.

Appellant argues in Part B. that, "[W]hen a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use." MPEP § 2165.02(c).

Note the, "correlate with the entire scope of the claim" requirement. A formulation that it has not been established can be made, and it has further not been established could be effective for its intended use, most certainly does not "correlate with the entire scope of the claim". Note that where Appellant cites the "teachings" of the specification said "teachings" comprise mere speculation as none of the working examples employ a "hybridoma" consisting of an APC and a virally infected cell.

Appellant admits that, "the examples were directed to tumor cells rather than virally infected cells", but then assets that, "there is no objective reason to doubt that the results would be similar for virally infected cells, because the same mechanism applies".

Appellant's assertion comprises no more than wishful thinking. "Objective reason" has been provided in the Frank et al. and Roberts references; the references teach that even if the claimed formulation could have been made, there were significant questions as to whether or not said formulation could have been employed for its intended use (*in vivo* treatment).

Appellant has not addressed the teachings of these references choosing rather to accuse the Examiner of "discounting" Appellant's evidence, i.e., Marañon et al.

Appellant's accusation is simply not true and, thus, does not comprise a compelling argument; the reference was addressed at page four of the Final Office action mailed 1/26/06. As set forth in that Office action:

> "…the publication comes some seven years after the priority date of the instant application, thus, it cannot be used to establish the enablement of the instant application as of its priority date. Second, the reference employs live antigen-loaded dendritic cells and not the fusion products of the instant claims. Also note that the reference addresses a number of issues that were clearly not known as of the priority date of the instant application, in particular, the manner in which dendritic cells take up and present antigens (note the use of the terms "unexpectedly" and "surprisingly"), a property that it is unclear whether or not the fusion products of the instant claims would possess".

In the instant Brief Appellant puzzlingly asserts that the Examiner's reasons, "are inapposite to Marañon's value in demonstrating the enablement of the claimed invention. It is well-established that a post-filing date reference can be used to demonstrate enablement when the reference merely demonstrates the state of the art as of the priority date."

As set forth above, the antigen-loaded APC of the reference is not the virally infected APC of the instant claims. As set forth in Pope et al., the manner in which dendritic cells take up and present antigens is critical to the T cell activation

properties. Clearly, the skilled artisan would readily see that antigen-loaded APCs take up and present exogenous (external) antigens in manner unrelated to the method required by the claimed formulation wherein the APC hybrids (if they could be produced) would be required to process endogenous viral (internal) antigens - this is basic cellular immunology. To the skilled artisan said difference in antigen processing comprises a huge difference in mechanisms that must be addressed and considered before broad conclusions such as, "the same mechanism applies" (instant Brief, page 6) could be credibly drawn. And note that Appellant agrees that it is the *"state of the art at the priority date"* that is key. Thus, the 2004 teachings of Marañon et al. tell us nothing about the state of the art at the instant application's 1997 filing date, other than that there were questions that had not yet been thought of to ask at that early date.

Appellant concludes by offering that even if the HIV embodiment is inoperative the claimed invention might still be enabled.

Appellant's conclusion might be compelling if the specification or art (prior- or post-filing) offered any evidence that the claimed formulations could either be made or employed for their intended use. Unfortunately, said evidence is lacking in this case.

(11) Related Proceeding(s) Appendix

Copies of the court or Board decision(s) identified in the Related Appeals and Interferences section of this examiner's answer are provided herein.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/G.R.Ewoldt/
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